Kindly make of record the attached Sequence Listing, in paper and disc formats.

REMARKS

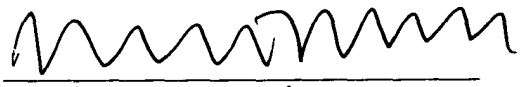
The communication mailed September 21, 2001, called for submission of a Sequence Listing, in paper and disc formats. The same is attached. Applicants hereby state that the content of the paper and disc formats is the same, and that these introduce no new matter into the present application.

The first five sequences are already identified in the text of the specification and claims as filed. Sequence ID No. 6 refers to the synthetic peptide on page 118 of the specification, and therefore the specification is amended accordingly.

Attached hereto is a marked-up version of the changes made to the specification. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

YOUNG & THOMPSON

By 

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October 22, 2001

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Paragraph beginning at line 24 of page 117 and continuing through the end of page 118 has been amended as follows:

The determination of the activity of thrombomodulin of an aqueous [prepraration] preparation is performed by observing the function of the preparation for accelerating the activation of protein C by thrombin (APC assay). Thus, 5 μ l of a sample solution, which was prepared suitable from an aqueous injection preparation containing a soluble thrombomodulin so that the thrombomodulin was contained therein, by an adequate dilution, in an amount in the range from 0.35 to 1.4 ng, are added to 37.5 μ l of a 50 mM Tris-HCl buffer solution (pH = 8.5) containing 100 mM NaCl, 3 mM calcium chloride, 0.1 % bovine serum albumin (supplied from the firm Sigma) and 0.225 NIHU of human thrombin (supplied from the firm Sigma) and the mixture is stood still for 15 minutes at 37 °C, whereto 7.5 μ l of bovine protein C of about 300 μ g/ml (supplied from the firm Life Technologies) are added and the resulting mixture is again stood still for 30 minutes at 37 °C in order to activate the protein C. Then, about 7.5 μ l of an aqueous solution containing about 100 μ l/ml of a heparin (supplied from Wako Pure Chemical Ind., Ltd.) and about 6 μ l/ml of Antithrombin III (of the firm Life Technologies) are added to the mixture to terminate the reaction. To this mixture are then

added 500 μ l of a solution containing 100 μ g/ml of a synthetic substrate (Boc-Leu-Ser-Thr-Arg-MCA) (SEQ ID NO: 6) and the resulting mixture is stood still for 20 minutes at 37°C. The substrate-scissoring reaction is then terminated by adding 50 μ l of acetic acid. The reaction mixture is examined by observing the fluorescence strength at an excitation wave length of 380 nm and at an emission wave length of 440 nm using a fluorescence spectrophotometer to determine the amount of the existing activated protein C, whereupon the thrombomodulin activity is calculated by comparison with a reference preparation of standard thrombomodulin activity.